5. Starr TB, Zacharewski T, Sutter T, Safe S, Greenlee W, Connolly R. Concerns with the use of a toxic equivalency factor (TEF) approach for risk assessment of "dioxin-like" compounds. Organohalogen Compounds 34:91–94 (1997).

van Leeuwen's Response

In our paper, "Toxic Equivalency Factors (TEFs) for PCBs, PCDDs, PCDFs for Humans and Wildlife" (*1*), we described the results of a World Health Organization (WHO) working group that evaluated the existing TEFs for human risk assessment and derived consensus TEFs for fish and birds.

Starr et al. comment on the approach taken for the derivation of TEFs as described in our paper (*1*) and criticize the inadequate characterization of the uncertainty of the TEFs. They state that the following sentence is the only uncertainty characterization:

> ... it is unlikely for the use of this additive model to result in a great deal of error in predicting the concentrations of TCDD TEQs or responses at environmentally relevant levels due to nonadditive interactions.

In addition, they request explicit quantitative estimates on the uncertainty in each REP value, each TEF, and on the deviation from parallelism for the different end points.

Their first statement is incorrect. In the paper we clearly stated that the TEFs that were derived are "an order of magnitude estimate." This is a clear illustration of the overall uncertainty in TEF values based on the differences in outcomes of the different end points and the variation in available data for the different congeners. In addition, Starr et al. misinterpreted the sentence quoted above. This sentence is based on the opinion of Van den Berg et al. (*1*) that the use of an additive model in the TEF approach, in contrast to including nonadditive (synergistic or antagonistic) effects, does not result "in a great deal of error."

Providing a quantitative estimate of the uncertainty of the individual REPs, as requested by Starr et al., is often not possible. Uncertainty in no-observed-(adverse)-effect levels [or lowest-observed-(adverse)-effect levels] or EC_{50} is usually not given in the studies used by the WHO working group. Therefore, a more qualitative, tiered approach was chosen to select the REP values in which we had greatest confidence, and not because we believe they are "without error." This weighted procedure is clearly outlined in the original paper. For those scientists who want to address the variation in REP values in more detail, the database containing all the information that was used in the derivation of TEFs is available on request. In their comments, Starr et al. suggestively stated that "the database is said to be available." The database was available directly after the WHO TEF meeting that was held in June 1997. Requests were received from several people, and all of them received the data.

Regarding their comment on the requirement of "parallelism of dose–response curves across end points" Starr et al. apparently failed to understand that the cascade of events following binding to the Ah receptor is different for each end point, which might thus result in different dose–response curves. Basic pharmacology and endocrinology have shown that multiple responses mediated by the same receptor mechanism do not have to have parallel dose–response curves because binding to a receptor is but the first step in the cascade of responses. Thus, per definition, the dose–response curves for different health end points cannot be expected to be parallel. This is one of the inherent uncertainties in the derivation of TEFs, but this is well recognized and covered adequately by Van den Berg et al. (*1*). Parallel dose–response curves are required for different congeners examining the same response, but this has been amply demonstrated in the literature for various dioxins, furans, and PCBs for various responses, and it was adequately covered by Van den Berg et al.

Where Starr et al. criticize the current approach and advocate the derivation of "species-, end point-, and dose-specific TEFs," it should be mentioned that the lack of information on dose–response relationships for all congeners, all end points/responses, and all species was just one of the reasons to develop the TEF methodology. It is highly unlikely that we could test all the congeners for all relevant end points and all species, including humans.

Finally, the TEF approach is a risk assessment tool; it was not developed to produce precise estimates of risk, but to approximate the toxic potency of exposure to a mixture of dioxin-like compounds. As such, it appears to work remarkably well. A large number of studies published in peer-reviewed literature have demonstrated a statistically highly significant correlation between TEQ levels in complex mixtures, derived by making use of TEFs, and predicted health outcomes in different animal species. An overview of this can be found in a series of articles in *Human and Ecological Risk Assessment,* Volume 5 (1999), in which several of these studies have been cited. Thus, we conclude that although the TEF approach might not be perfect because of its inherent uncertainties, no valid alternative for risk assessment purposes currently exists.

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References and Notes

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Safe Food: Should We Be Afraid?

I would like to comment on the article "Safe Food: An All-consuming Issue" (*1*). I consider this article to be scaremongering. Scaremongering, a very real and increasingly dangerous problem, often with total disregard to the truth, has become a major, and obviously profitable, growth industry wherein "nonprofit" organizations and various individuals prosper at the expense of the credulous public. Just how credulous can the public be? This week I had a vivid example when my wife of 55 years, on the basis of a recent article, told me she would no longer serve me meat products such as salami and summer sausage, which I have been happily consuming for most of my life!

True, meat contamination by such organisms as *Salmonella* and new virulent mutant strains of *Escherichia coli* kills many people every year, usually in fresh ground meat. These deaths are totally avoidable by the appropriate use of irradiation. I have worked with or studied food irradiation since 1950 and know that, worldwide, hundreds of investigations have shown food irradiation to be totally effective and completely safe.

Yet Schmidt cites Food and Water merely as a "nonprofit advocacy organization." How could he! This is the organization that spends quite extraordinary amounts of money proclaiming that anyone who eats irradiated foods is likely to have severely deformed children (among other horrors).

I could fill many pages with accounts of encounters with some these dangerous frauds, and over the years I have written several articles on the topic of scaremongering in the food industry (*2–4*).

I am old (81) and long retired (since 1982), and I profoundly hope that sometime soon a publication such as *EHP* will give the same concern to this scandal as you would to any other virulent epidemic. Thank you for this chance to blow off some steam.